Immunology of Guillain-Barré Syndrome

Israel Steiner and Oded Abramsky

The Department of Neurology, Hadassah University Hospital, Hebrew University Hadassah Medical School, Jerusalem, Israel 91120

Introduction

Guillain-Barré syndrome (GBS) is a defined clinical entity which was first described in 1859 by Landry [64] and in 1916 by Guillain, Barré, and Strohl [46]. In its classical form the disease is monophasic and consists of acute or subacute progressive ascending motor weakness, sometimes culminating in quadriplegia. Deep tendon reflexes are reduced or absent and sensory symptoms and signs are usually mild. Characteristically, protein level in the cerebrospinal fluid (CSF) is elevated, with no or very few cells present. The annual incidence of GBS is between 0.6 [22] and 1.9 [29, 112] per 100,000 population. Distribution is world-wide and it occurs at all ages with minor peaks in young adults and in the fifth decade [58]. In most cases disease progression is arrested within 2 to 4 weeks followed by slow recovery in 80–90% of patients. Hospitalization may sometimes be very long and complicated by intubation and tracheostomy, infections, pulmonary embolus, and psychologic depression. With intensive care facilities mortality rate is 1–3% [96] and is mainly due to respiratory failure and autonomic complications. Approximately 3–5% of GBS patients have relapse(s) appearing after a symptom-free interval of a few weeks and up to 20–30 years in rare instances.

Patients sometimes present with unusual clinical features which make diagnosis difficult. Auxiliary studies, namely electrodiagnosis and sural nerve biopsy, as well as follow-up, are then needed to establish the diagnosis of GBS. Despite restrictive criteria for diagnosis set forth in 1978 by the Ad Hoc NINCDS Committee [13], there are quite different clinical syndromes which are considered by some as variants of GBS: (a) the syndrome of ophthalmoplegia, ataxia, and areflexia (the Miller Fisher syndrome)[44]; (b) the syndrome of sensory loss and areflexia [111]; (c) polineuritis cranialis, and (d) chronic demyelinating inflammatory polyneuropathy (CDIP). In CDIP the same symptomatology as in GBS develops over months and years in a steady progressive, stepwise, or progressive relapsing form. Laboratory, electrodiagnostic, and histopathologic findings are sometimes indistinguishable.
from the finding in acute GBS [36]. Peak incidence is in the fifth and sixth decades, and prognosis is less favorable than GBS. In one series [42] 53 patients were followed for a mean of 7.4 years. Only 4% recovered while 28% were confined to bed or a wheelchair and 11% died. Whether all these clinical syndromes have a common pathogenesis is unknown and there is no reliable diagnostic marker shared by them.

Pathology

In 1949, Haymaker and Kernohan [49] described autopsy findings in 50 patients with GBS. They concluded that "study of the central nervous system revealed nothing of consequence in the spinal cord, brain stem, or cerebrum. The peripheral nervous system on the other hand was consistently affected, the lesions being concentrated in the spinal nerves, i.e., in the region where the anterior and posterior roots fuse and extending for a short distance proximally and distally". The presence of inflammatory cells "were regarded as part of the reparative process". In 1969 Asbury et al. [12] detected inflammatory cells in the nerves of 19 patients who died of GBS, and the cells were present from the earliest stages of disease. Myelin destruction was confined to loci of nerve roots which were infiltrated by the inflammatory cells. Since then microscopic and ultrastructural studies of both autopsy material and nerve biopsies obtained from patients with GBS confirmed the observation that primary demyelination occurs only in tissues harboring the inflammatory cells [20, 57, 90, 92]. To summarize the present knowledge of the pathology of GBS; it is a neuropathy consisting of inflammatory lesions scattered throughout the peripheral nervous system (PNS) where myelin is lost in the presence of lymphocytes and macrophages [91]. Hence the synonymous term of demyelinating inflammatory polyradiculoneuropathy (DIP).

Electrophysiologic Studies

Abnormal electrophysiologic findings are present in up to 90% of patients [75]. The likelihood of detecting electrophysiologic pathology increases with the number of nerves studied. This is attributed to the patchy distribution of demyelination. Findings parallel clinical signs and course of GBS only grossly or not at all [76]. The abnormalities include decreased motor conduction velocities and increased motor distal latencies. The sensory nerve action potentials are reduced. F-wave studies and somatosensory evoked potential recordings may detect involvement of nerve roots and proximal segments of the PNS [47, 59]. When spontaneous activity is present on electromyography, it is regarded as a result of secondary axonal involvement and is associated with a poor prognosis for complete recovery [96].

Immunopathology

The evidence that the clinical pathologic entity of GBS is immune mediated is based on clinical considerations, laboratory findings, and experimental models. Fifty to